REMARKS

The Applicant expresses appreciation to the Examiner for consideration of the subject patent application.

Therefore, this amendment is in response to the Final Office Action mailed January 05, 2005. Claims 1 and 60 have been amended to overcome the rejections under 35.U.S.C. §112, second paragraph, set forth in this Office Action. The claims are amended to be more specific in describing the present invention and the support for them can be found throughout the specification, i.e. page 17-18 and Figure 8. No new matter is added. Claim 59 and Claim 67 are cancelled without prejudice.

Claim Rejections - 35 U.S.C. § 112

The Examiner alleges that Claims 49, 59 and 67 are vague and indefinite. Claim 49 is amended to address the issues raised by the Examiner and claims 59 and 67 are cancelled. Therefore, it is respectfully submitted that the rejection should be withdrawn in light of the claim amendments.

Claim Rejections - 35 U.S.C. § 103

Claims 60-67 (including independent claim 60) were rejected under 35 U.S.C. § 103 as being unpatentable over Czech et al. (US 6,194,173)(hereafter referred as "Czech") in view of Boguslaski et al. (US Patent 5,420,016) (hereafter referred as "Boguslaski").

In order to most succinctly explain why the claims presented herein are allowable, the Applicant will direct the following remarks primarily to independent claim 60 with the understanding that once an independent claim is allowable, all claims depending therefrom are allowable.

The applicant respectfully submits that the presently submitted claims are not obvious in view of the references cited. In other words, one of ordinary skill in the art, when combining all teachings of the references of record at the time of the invention was made, would not have been motivated to come up with the presently claimed invention.

The initial burden is on the Examiner to establish a case of *prima facie* obviousness. The test for establishing such a case is well stated in *In re Vaeck*, 947 F.2d 488, 20USPQ2d 1438

(Fed. Cir.1991) as follows:

> "To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and reasonable expectation of success must both be found in the prior art, and not based on the applicant's disclosure."

When applying 35 U.S.C. 103, the following tenets of patent law must be adhered to: (A) the claimed invention must be considered as a whole; (B) the references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination; (c) the references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and (D) reasonable expectation of success is the standard with which obviousness is determined. Hodosh v. Block Drug Co., Inc., 786 F.2d 1136, 1143 n.5, 229 USPQ 182,187 n.5 (Fed. Cir. 1986)

Under this statement of law, the Applicants respectfully submit that the present invention would not be obvious over Czech in view of Boguslaski.

Czech discloses Grp1 as an adaptor for membrane signaling. The patent describes nucleic acid molecules, recombinant expression vectors for the expression of Grp1, host cell lines containing these expression vectors, transgenic animals in which the Grp1 gene has been disrupted, transgenic animals engineered for expression of recombinant Grp1, Grp1 proteins, including fusion proteins, and anti-Grp1 antibodies. Characterization of genetic mutations of Grp1 in patients is also disclosed. The patent describes methods of modulating cell adhesion by modulating the activity of Grp1 and it's interaction with products of PI 3-K, including $PI(3,4,5)P_3$, or modulating the interaction of Grp1 with integrins. The patent also discloses a

screening assay for testing compounds for modulation of or interference with the interaction of Grp1 with $PI(3,4,5)P_3$ using a reaction mixture containing PI(3,4,5)P3, Grp1, and a test compound.

The screening assay described in Czech differs from the present invention in that it is not presented as a kit to be used in a method for detecting production of $PI(3,4,5)P_3$ produced by enzymatic activity of PI 3-kinase. The PI 3-kinase assay kit and the method of using thereof involves exposure of a $PI(3,4,5)P_3$ specific binding protein to an analyte solution produced by the reaction of $PI(4,5)P_2$ substrate with PI 3-kinase. Thus, unlike the reaction mixture described by Czech, the PI 3-kinase assay kit of the present invention contains a mixture of the enzyme substrate $PI(4,5)P_2$ and the enzyme product, $PI(3,4,5)P_3$. Unlike Czech, the assay method of the present invention involves measurement of enzyme activity by quantitation of $PI(3,4,5)P_3$ present in the analyte using a competitive assay in which the $PI(3,4,5)P_3$ present in the analyte solution competes for the interaction of the lipid binding protein with a labeled $PI(3,4,5)P_3$ probe to produce a change in signal which correlates with the amount of $PI(3,4,5)P_3$ present in the analyte, which in turn provides a measure of the PI 3-kinase enzyme activity. Thus, the specificity of the lipid binding protein for $PI(3,4,5)P_3$ when exposed to a mixture containing $PI(4,5)P_2$ and $PI(3,4,5)P_3$ is used as a tool to measure the amount of $PI(3,4,5)P_3$ produced by enzymatic conversion of $PI(4,5)P_2$ by PI 3-kinase. Thus, the PI-3 kinase assay kits and the PI-3 kinase assay methods disclosed in the present invention are fundamentally different than those disclosed by Czech et al. In addition, nothing in Czech teaches or suggests using Grp1 as a specific detector for a lipid or to determine the activity of a lipid kinase. Therefore, the present invention differs from Czech because the present invention relates to the determination of lipid kinase activity, while Czech relates to a lipid binding protein. Nothing in Czech discloses or teaches a kit and a method for determining lipid kinase activity method as claimed in the present invention.

Boguslaski describes a very different type of invention which is not related to either the methods described in Czech or the methods disclosed in the present invention. This patent discloses a test device for detecting the presence of *Heliobacter pylori* in biological tissue specimens. The test device is a multilayer strip-like device which contains diffusion membranes and is designed for separation of components present in the biological sample and measurement of urease activity in the sample as an indicator that the bacteria is present. The patent describes

test kits which include the test device, a holder, a rehydrating solution, and a substrate element, which is comprised of a filter paper impregnated with urea. The assay and the test kits differ considerably in purpose, design, underlying principles, and detection methods from those that we disclose. The only common element appears to be the word "kit".

The examiner argues that combination of Czech with Boguslaski makes it obvious that one could assemble the various reagents and components described by Czech into a kit as described in Boguslaski. However, the methods and components described by Czech et al. are fundamentally different from those presented in Boguslaski. One could not use the methods or the device presented in Boguslaski, which describes procession of biological samples and detection of a biomarker for the presence of bacteria, as a guide for assembling test kits based on the material disclosed by Czech.

There is no motivation to combine the Czech and the Boguslaski references. The references teach away from each other because Boguslaski teaches methods for detecting the presence of *Heliobacter pylori* in biological tissue specimens, while Czech teaches cloning and purifying Grp1 proteins. Czech discloses methods of modulating Grp1 activity which is not in any way related to methods for detecting small quantities of analytes as taught by Boguslaski. Therefore, it is respectfully submitted that there is no motivation for one skilled in the art to combine the teachings of Boguslaski and Czech.

In addition, the Boguslaski and Czech references, when combined, still do not teach or suggest the elements of the independent claim 60. Specifically, the Boguslaski reference does not teach the elements of an anylyte solution for assaying PI-3 kinase containing a protein, having a phosphoinositide lipid recognition motif that interacts with a target lipid and a competing phosphoinositide lipid, which is labeled by a non-radioactive signal. Therefore, it is respectfully submitted that the Examiner has failed to establish a case of *prima facie* obviousness because: first, there is no suggestion or motivation to modify the reference or to combine reference teachings; second, there is no reasonable expectation of success and finally, the prior art references, even when combined, still fail to teach or suggest all the limitations as claimed in the present invention. Therefore, the Applicant respectfully submits that Claims 60-66 are allowable.

CONCLUSION

In light of the above, the Applicant respectfully submits that pending claims are now in condition for allowance. Therefore, the Applicant requests that the claims be allowed and passed to issue. If any impediment to the allowance of these claims remains after entry of this Amendment, the Examiner is strongly encouraged to call Weili Cheng Ph.D, or in her absence, the undersigned at (801) 566-6633 so that such matters may be resolved as expeditiously as possible.

The Commissioner is hereby authorized to charge any additional fee or to credit any overpayment in connection with this Amendment to Deposit Account No. 20-0100.

DATED this 4th day of April, 2005.

Respectfully submitted,

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